In This Issue ......................................................... 469

Meet the First Authors ............................................. 470

Editorials

New Initiatives to Improve the Rigor and Reproducibility of Articles
Published in Circulation Research
Roberto Bolli .......................................................... 472

Allele-Specific Gene Silencing: Another Step in the Inexorable Advance of Gene Therapy for Cardiac Arrhythmia Management
Stanley Nattel ......................................................... 480

When High Throughput Meets Mechanistic Studies: A State-of-the-Art Approach in Brugada Syndrome
Bettina Heidecker .................................................. 483

Besides Imprinting: Meg3 Regulates Cardiac Remodeling in Cardiac Hypertrophy
Shizuka Uchida ........................................................ 486

Trainee and Young Investigator Corner

Training for Success
Robert N. Correll .................................................... 488

Promising Young Investigators

Michael Potente: No Time to Waste
Ruth Williams ......................................................... 490

News & Views

Cardiovascular Research in Germany
Gerd Heusch, Thomas Eschenhagen, Stefanie Dimmeler .............................. 492

CIRCULATION RESEARCH (ISSN 0009-7330 print / 1524-4571 online) is published semimonthly for 24 total issues a year by Wolters Kluwer Health, Inc. at 14700 Citicorp Drive, Bldg 3, Hagerstown, MD 21742. Business offices are located at Two Commerce Square, 2001 Market Street, Philadelphia, PA 19103. Production offices are located at 351 West Camden Street, Baltimore, MD 21201-2436. Individuals may subscribe for their personal use at the following rates for print subscriptions: $225 for AHA/ASA Domestic and International Members (excluding General Membership level), or $790 for domestic non-members and $937 for international non-members. AHA membership information can be found online at professional.heart.org. Periodicals postage paid at Hagerstown, MD, and additional mailing offices. POSTMASTER: Send address changes to Circulation Research, American Heart Association, Wolters Kluwer Health, Inc., PO Box 1610, Hagerstown, MD 21740.
**Viewpoints**

Large Animal Model Efficacy Testing Is Needed Prior to Launch of a Stem Cell Clinical Trial: An Evidence-Lacking Conclusion Based on Conjecture
Stephen E. Epstein, Dror Luger, Michael J. Lipinski .................................................. 496

Application of PCSK9 Inhibitors in Practice Challenges and Opportunities
Tina M. Kaufman, P. Barton Duell, Jonathan Q. Purnell, Cezary Wójcik, Sergio Fazio, Michael D. Shapiro .................................................. 499

**Molecular Medicine**

Genetic Deletion of NADPH Oxidase 1 Rescues Microvascular Function in Mice With Metabolic Disease

ARHGAP18 Protects Against Thoracic Aortic Aneurysm Formation by Mitigating the Synthetic and Proinflammatory Smooth Muscle Cell Phenotype
Renjing Liu, Lisa Lo, Angelina J. Lay, Yang Zhao, Ka Ka Ting, Elizabeth N. Robertson, Andrew G. Sherrah, Sorour Jarrahi, Haibo Li, Zhaoxiong Zhou, Brett D. Hambly, David R. Richmond, Richmond W. Jeremy, Paul G. Bannon, Mathew A. Vadas, Jennifer R. Gamble .................................................. 512

**Cellular Biology**

**Allele-Specific Silencing of Mutant mRNA Rescues Ultrastructural and Arrhythmic Phenotype in Mice Carriers of the R4496C Mutation in the Ryanodine Receptor Gene (RYR2)
Rossana Bongianino, Marco Denegri, Andrea Mazzanti, Francesco Lodola, Alessandra Vollero, Simona Boncompagni, Silvia Fasciano, Giulia Rizzo, Damiano Mangione, Serena Barbaro, Alessia Di Fonso, Carlo Napolitano, Alberto Auricchio, Feliciano Protasi, Silvia G. Priori .................................................. 525

**The Brugada Syndrome Susceptibility Gene HEY2 Modulates Cardiac Transmural Ion Channel Patterning and Electrical Heterogeneity

**Transient Notch Activation Induces Long-Term Gene Expression Changes Leading to Sick Sinus Syndrome in Mice
Yun Qiao, Catherine Lipovsky, Stephanie Hicks, Somya Bhatnagar, Gang Li, Aditi Khandekar, Robert Guzy, Kel Vin Woo, Colin G. Nichols, Igor R. Efimov, Stacey Rentschler .................................................. 549

Sirt3 Impairment and SOD2 Hyperacetylation in Vascular Oxidative Stress and Hypertension

**Role of Hey2 in Transmural Electrical Patterning**
Veerman *et al.* page 537

**Notch and Sick Sinus Syndrome**
Qiao *et al.* page 549

**Inactivation of Sirt3 and SOD2 in Hypertension**
Dikalova *et al.* page 564
Inhibition of the Cardiac Fibroblast–Enriched lncRNA Meg3 Prevents Cardiac Fibrosis and Diastolic Dysfunction

Maria-Teresa Piccoli, Shashi Kumar Gupta, Janika Viereck, Ariana Foinquinos, Sabine Samolovac, Freya Luise Kramer, Ankita Garg, Janet Remke, Karina Zimmer, Sandor Batkai, Thomas Thum

Letters to the Editor

Letter by El-Battrawy et al Regarding Article, “The Brugada Syndrome Susceptibility Gene HEY2 Modulates Cardiac Transmural Ion Channel Patterning and Electrical Heterogeneity”

Ibrahim El-Battrawy, Siegfried Lang, Martin Borggrefe, Xia-Bo Zhou, Ibrahim Akin

Response by Veerman et al to Letter Regarding Article, “The Brugada Syndrome Susceptibility Gene HEY2 Modulates Cardiac Transmural Ion Channel Patterning and Electrical Heterogeneity”

Christiaan C. Veerman, Ronald Wilders, Arthur A. Wilde, Ruben Coronel, Carol Ann Remme, Arie O. Verkerk, Connie R. Bezzina

In June 2017, the average time from submission to first decision for all original research papers submitted to Circulation Research was 12.45 days.

On the Cover: Volcano plot of HEY2 coexpression analysis in human left ventricular tissue. Genes that are coexpressed with HEY2 in human heart were identified by correlating the abundance of transcripts genome-wide with the abundance of the HEY2 transcript (x-axis, regression coefficient; y-axis, negative log of the P value). The transcript of the KCNIP2 gene, which encodes potassium channel interacting protein 2, was strongly positively correlated with that of HEY2. See related article, page 537.